

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A crystal ~~comprising at least 150 amino acid residues~~ of the Liver X receptor beta LXR β ligand binding domain (LXR β LBD) selected from the group consisting of:

(a) a crystal belonging to space group P2₁2₁2₁, wherein said LXR β LBD consists essentially of the amino acid sequence from Leu220 to Glu461 or Gly213 to Glu461 of a human LXR β shown in Figure 5a (SEQ ID NO: 1); and

(b) a crystal belonging to space group P6₁22, wherein said LXR β LBD comprises the amino acid sequence from Leu220 to Glu461 of a human LXR β shown in Figure 5a (SEQ ID NO: 1), or a polypeptide comprising an amino acid sequence at least 95% identical to the sequence from Leu220 to Glu461 of human LXR β (SEQ ID NO:1), wherein said polypeptide is capable of binding to an LXR β ligand, said LXR β ligand being chosen from N-(2,2,2-trifluoroethyl)-N-[4[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-benzenesulfonamide, 3-(3-(2-chloro-3-trifluoromethylbenzyl)-2,2-diphenylethylamino)propoxy)phenylacetic acid, 24(S),25-epoxycholesterol, or N-[1-(2-furanyl)ethyl]-N-4-pyridinyl-tricyclo[3.3.1.1^{3,3}.1^{3,7}]decane-1-carboxamide.

2. (Currently Amended) ~~A~~ The crystal according to claim 1, wherein the LXR β LBD crystal belonging to space group P6₁22 ~~comprising~~ comprises the amino acid sequence from Leu220 to Glu461 of a human LXR β shown in Figure 5a (SEQ ID NO: 1), ~~or an amino acid sequence having at least 95% identity with the sequence and which encodes for a LXR β ligand binding domain.~~

3. (Currently Amended) A The crystal according to claim 1, further comprising N-(2,2,2-trifluoroethyl)-N-[4[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-benzenesulfonamide bound to the LXR β LBD, the entire LXR β ligand binding domain.

4. (Currently Amended) A The crystal according to claim 1 or 3, wherein said crystal belongs to space group P2₁2₁2₁ and has the unit cell dimensions a = 59 +/- 3 Å, b = 100 +/- 5 Å, c = 176 +/- 3 Å, or a = 58.7 Å, b = 103.3 Å, c = 176 Å, wherein $\alpha = \beta = \gamma = 90^\circ$, produced using a sequence including helix 12 of LXR β .

5. (Currently Amended) A The crystal according to claim 1 or 3, wherein said crystal belongs to space group P6₁22 and has the unit cell dimensions a = b = 58.7 Å, c = 293.8 Å, $\alpha = \beta = 90^\circ$, $\gamma = 120^\circ$, usable in X-ray crystallography.

6. (Currently Amended) A The crystal according to claim 1 or 3, further comprising 3-(3-(2-chloro-3-trifluoromethylbenzyl)-2,2-diphenylethylamino)propoxy)phenylacetic acid bound to the LXR β LBD, including a ligand bound to LXR β or a portion thereof.

7. (Currently Amended) A The crystal according to claim 6, wherein said crystal belongs to space group P6₁22 and has the unit cell dimensions a = 59 +/- 3 Å, b = 59 +/- 3 Å, c = 294 +/- 3 Å, or a = 58.7 Å, b = 98.9 Å, c = 175.8 Å, wherein $\alpha = \beta = 90^\circ$, $\gamma = 120^\circ$, in which the ligand is T0901317, GW3965 or any other ligand that binds with an affinity of $IC_{50} < 1000$ nM to the internal LXR β binding cavity.

8. (Currently Amended) A crystal of the Liver X receptor beta ligand binding domain (LXR β LBD) LXR β LBD belonging to the space group P2₁2₁2₁ and having the unit cell dimensions a = 59 +/- 3 Å, b = 100 +/- 5 Å, c = 176 +/- 3 Å, $\alpha = \beta = \gamma = 90^\circ$.

9. (Currently Amended) A crystal of Liver X receptor beta ligand binding domain (LXR β LBD) LXR β LBD belonging to the space group P6₁22 and having the unit cell dimensions $\alpha = 59 +/- 3 Å$, b = 59 +/- 3 Å, c = 294 +/- 3 Å, $\alpha = \beta = 90^\circ$, $\gamma = 120^\circ$.

10. (Currently Amended) A crystal of Liver X receptor beta ligand binding domain (LXR β LBD) ~~LXR β LBD~~ in complex with a coactivator peptide (TIF2 NR box 1 of TIF2) belonging to the space group P2₁2₁2 and having the unit cell dimensions $a = 89 \pm 3 \text{ \AA}$, $b = 91 \pm 3 \text{ \AA}$, $c = 131 \pm 3 \text{ \AA}$, $\alpha = \beta = \gamma = 90^\circ$.

11. (Previously Presented) A crystal according to claim 1, having a resolution determined by X-ray crystallography of better than 3.6 \AA .

12. (Original) A crystal according to claim 11 having a resolution determined by X-ray crystallography of better than 2.9 \AA .

13. – 28. (Canceled)

29. (Currently Amended) A crystallized molecule or molecular complex comprising a binding pocket defined by the ~~structure~~ structural coordinates of human Liver X receptor beta LXR β ligand binding domain (LXR β LBD) comprising amino acid residues Ser242, Phe268, Phe271, Thr2n, Leu274, Ala275, Ser278, Ile309, Met312, Leu313, Glu315, Thr316, Arg319, Ile327, Phe329, Leu330, Tyr335, Phe340, Leu345, Phe349, Ile350, Ile353, Phe354, His435, Gln438, Val439, Leu442, Leu449, Leu453, and Trp457, according to ~~the co-ordinate tables~~ the structural coordinates of the complex of LXR β LBD and 3-(3-(2-chloro-3-trifluoromethylbenzyl-2,2-diphenylethylamino)propoxy)phenylacetic acid as shown in Table 2, or a homologue of said molecule or molecular complex wherein said homologue has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 \AA .

30. (Currently Amended) A crystallized molecule or molecular complex comprising a binding pocket defined by the structural coordinates of human Liver X receptor beta-composition comprising at least 150 amino acid residues of the LXR β ligand-binding domain (LXR β LBD) comprising amino acid residues Ser242, Phe268, Phe271, Thr2n, Leu274, Ala275, Ser278, Ile309, Met312, Leu313, Glu315, Thr316, Arg319, Ile327, Phe329, Leu330, Tyr335, Phe340,

Leu345, Phe349, Ile350, Ile353, Phe354, His435, Gln438, Val439, Leu442, Leu449, Leu453, and Trp457, according to the complex LXR β LBD and N-(2,2,2-trifluoroethyl)-N-[4[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-benzenesulfonamide as shown in Table 2, or a homologue of said molecule or molecular complex having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å.

31. (Previously Presented) An isolated protein consisting essentially of the amino acid sequence shown from amino acid 220 to amino acid 461 in Figure 5a (SEQ ID NO: 1) or the sequence shown in Figure 5b (SEQ ID NO: 2).

32. (Original) An isolated protein according to claim 31, additionally comprising a tag, such as a his-tag.

33. – 34. (Canceled)

35. (Previously Presented) An isolated protein having an amino acid sequence identical to the amino acid sequence used in a crystal according to claim 1.

36. – 39. (Canceled)

40. (New) A crystal of the Liver X receptor beta ligand binding domain (LXR β LBD) in complex with a coactivator peptide (NR box 1 of TIF2), wherein:

said crystal belongs to space group P2₁2₁2₁; and

said LXR β LBD comprises the amino acid sequence from Leu220 to Glu461 of a human LXR β shown in Figure 5a (SEQ ID NO: 1), or a polypeptide having an amino acid sequence at least 95% identical to the sequence from Leu220 to Glu461 of a human LXR β (SEQ ID NO:1), wherein said polypeptide is capable of binding to an LXR β ligand, said LXR β ligand being chosen from N-(2,2,2-trifluoroethyl)-N-[4[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-benzenesulfonamide, 3-(3-(2-chloro-3-trifluoromethylbenzyl)-2,2-diphenylethylamino)propoxy)phenylacetic acid, 24(S),25-epoxycholesterol, or N-[1-(2-

furanyl)ethyl]-N-4-pyridinyl-tricyclo[3.3.1.1^{3,7}]decane-1-carboxamide Liver X receptor beta ligand binding domain (LXR β LBD).

41. (New) The crystal of LXR β LBD of claim 40, wherein the LXR β LBD comprises the amino acid sequence from Leu220 to Glu461 of a human LXR β shown in Figure 5a (SEQ ID NO: 1).

42. (New) The crystal of LXR β LBD of claim 41, said crystal having space group P2₁2₁2 and having the unit cell dimensions $a = 89 \pm 3$, $b = 91 \pm 3$, $c = 131 \pm 3$, $\alpha = \beta = \gamma = 90^\circ$.

43. (New) The crystallized molecule or molecular complex of claim 29 or 30, wherein said binding pocket was resolved by molecular replacements using the structure of a thyroid hormone receptor as a search model.

44. (New) The crystallized molecule or molecular complex of claim 29, wherein the complex of LXR β LBD and 3-(3-(2-chloro-3-trifluoromethylbenzyl-2,2-diphenylethylamino)propoxy)phenylacetic acid has the structural coordinates according to Table 2, or a homologue of said molecule or molecular complex having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å.

45. (New) The crystallized molecule or molecular complex of claim 30, wherein the complex of LXR β LBD and N-(2,2,2-trifluoroethyl)-N-[4[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-benzenesulfonamide has the structural coordinates according to Table 2, or a homologue of said molecule or molecular complex having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5 Å.